Remarks

Claims 15, 16, 28, and 29 are pending. By the above amendment, the claims have been amended without adding new matter to incorporate helpful suggestions of the Examiner to more clearly define the invention, as further discussed below.

In the outstanding Office Action, the Examiner objected to claim 28 due to a typographical error. By the above amendment to claim 28, this objection has been overcome.

The Examiner rejected claims 15, 16, and 28 under 35 U.S.C. § 112, first paragraph, as supposedly lacking enablement for the full scope of the claimed subject matter. The Examiner argued that, since no compounds augmenting serine C-E protease activity are known, the specification does not enable the claimed assay method for identifying all modulators, as opposed to just inhibitors. Since independent claim 15 has now been written to more particularly define the method as useful for identifying inhibitors, this ground of rejection has been obviated.

Claims 15 and 16 were also rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. In particular, the Examiner indicated that claim 15 lacked reference to a control. In accordance with one of the Examiner's alternative suggestions, the independent claim has been amended to refer to comparison with a control. Additionally, the Examiner indicated that claim 16 was indefinite in reciting an improper Markush group, in that one species (FRET assay) was a subset of another (fluorogenic assay) and that another species (radiometric assay) entailed an additional step not expressly recited. As suggested by the Examiner, the recitation of a FRET assay has been moved to a new dependent claim. And the recitation of the radiometric assay has been deleted to remove this basis for rejection. The rejection for indefiniteness has therefore been overcome.

Claims 15, 16, and 28 were also rejected based on new grounds under 35 U.S.C. § 103(a). Specifically, these claims were rejected on the following alternative combinations of references: Botstein et al. (WO 99/35170) in view of Nelson et al. (U.S. Patent No. 5,242,463); Chen et al. (WO 99/14328) in view of Nelson et al.; and Antalis et al. (WO 98/36054) in view of Nelson et al. These rejections are respectfully traversed.

The disclosures of none of the Botstein et al., Chen et al., and Antalis et al. references, alone or coupled with the newly cited Nelson et al. reference, teaches or suggests the assay method as defined in each of the present claims. As previously pointed out, none of the primary references teaches or suggests a method for identifying inhibitors of serine protease C-E comprising using an assay reagent comprising an amino acid sequence as set forth in SEQ ID NO:8 as defined by the claims. The Nelson et al. reference fails to cure this deficiency. Indeed, the secondary reference was cited in the rejections not for any purported teaching or suggestion for employing the fusion polypeptide of SEQ ID NO:8 in an assay method, but for certain teachings regarding features of fluorogenic assays in general.

With respect to the use of a serine protease C-E comprising a catalytic domain amino acid sequence as set forth in SEQ ID NO:8 as recited in the present claims, the Examiner relied on the primary references in an attempt to establish obviousness. The Examiner argued in each of the Section 103 rejections at pages 5-9 of the Office Action that the proteolytic activity of the catalytic domain of the native PRO343/C-E catalytic domain released by post-translational processing is indistinguishable from the proteolytic activity of the catalytic domain of the fusion polypeptide of SEQ ID NO:8 in assays as claimed, absent a showing otherwise by Applicant.

Contrary to the Examiner's assertion, however, an assay method employing the sequence of the native protease is not inherently the same as an assay employing the sequence of the fusion polypeptide as claimed. As acknowledged in the Examiner's introductory comments at page 2 of the detailed Office Action, the two polypeptides are different. Accordingly, methods employing the two distinct assay reagents are different, regardless of whether or not both methods are useful to identify compounds having the same ultimate activity.

In determining obviousness of a claimed method, the question is not whether the result of the method would have been obvious from the prior art, but whether the method itself would have been obvious. The burden is not on Applicant to show that the measured change in labeled substrate in the claimed method differs from a measured change in an assay method of the prior art, but on the Examiner to show how and why it

would have been obvious to select an assay reagent comprising the claimed fusion polypeptide in place of the serine proteases disclosed in the references. Since this has not been shown, a proper *prima facie* case of obviousness has not been established and the Section 103 rejections should therefore be withdrawn.

In light of the foregoing, Applicant respectfully requests allowance of the pending claims.

Respectfully submitted,

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Linda S. Evans
Reg. No. 33,873

Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, New Jersey 08933-7003
(858) 320-3406